

ARTIFICIAL METALLOENZYMES FOR IN VIVO CATALYSIS: CHALLENGES AND OPPORTUNITIES

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Artificial metalloenzymes (ArMs) result from the incorporation of a catalyst precursor within a host protein, Figure 1. The resulting hybrid catalysts display features that are reminiscent of both homogeneous catalysts and enzymes. The optimization of the catalytic performance of ArMs is achieved by combining both chemical- and genetic means. The versatility of this chemo-genetic optimization strategy will be illustrated with selected examples including: transfer-hydrogenation, C–H activation, olefin metathesis, hydroamination etc, Figure 1. With the aim of integrating artificial metalloenzymes *in vivo*, the second part of the talk will present our efforts to combine ArMs with natural enzymes to mimic essential features of the metabolism including: cascade reactions as well as up- and cross-regulation. Having identified the critical metabolites leading to ArM's inhibition, our efforts towards engineering enzyme cascades *in vivo* will be summarized.

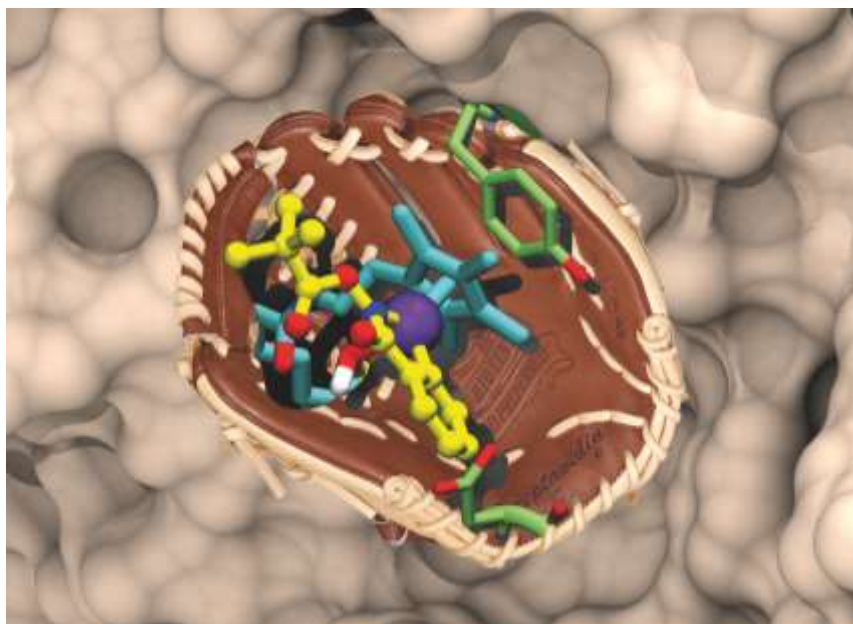


Figure 1 – Anchoring a catalyst precursor (ball & stick representation) within a host protein (baseball glove) affords an artificial metalloenzyme. The catalytic performance of the resulting hybrid catalyst can be optimized by chemo-genetic means: variation of the nature and position of the cofactor (turquoise stick representation) and mutation of aminoacid residues (green stick representation).

Reaction implemented
Hydrogenation
Transfer hydrogenation
Hydroamination
Allylic substitution
Suzuki cross-coupling
Dihydroxylation
Sulfoxidation
Alcohol oxidation
Peroxidation
Olefin metathesis
C–H activation
Cyclopropanation
Michael addition
Enzyme cascades